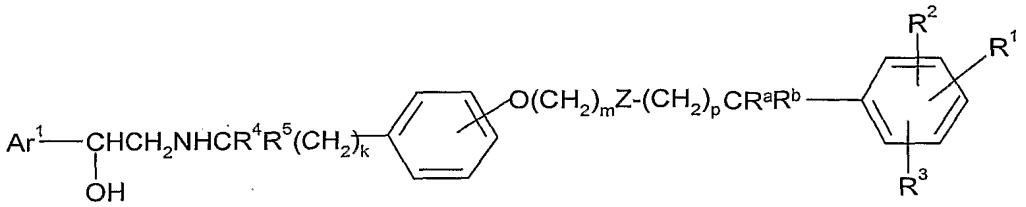
CLAIMS

A compound of formula (I)



(I)

or a salt, solvate, or physiologically functional derivative thereof, wherein:

k is an integer of from 1 to 3;

m is an integer of from 2 to 4;

p is an integer of from 0 to 3;

Z is O or CH_2-

R^1 is selected from hydrogen, C_{1-6}alkyl, hydroxy, C_{1-6}alkoxy, cyano, nitro, halo, C_{1-6}haloalkyl, XCO_2R^8, $-XC(O)NR^7R^8$, $-XNR^6C(O)R^7$, $-XNR^6C(O)NR^7R^8$, $-XNR^6C(O)NC(O)NR^7R^8$, $-XNR^6SO_2R^7$, $-XSO_2NR^9R^{10}$, XSR^6, $XSOR^6$, XSO_2R^6, $XNR^6SO_2NR^7R^8$, $XNR^6SO_2NR^7COOR^7$, $-XNR^7R^8$, $-XNR^6C(O)OR^7$,

or R^1 is selected from -X-aryl, -X-hetaryl, or -X-(aryloxy), each optionally substituted by 1 or 2 groups independently selected from hydroxy, C_{1-6}alkoxy, halo, C_{1-6}alkyl, C_{1-6}haloalkyl, $-NR^6C(O)R^7$, SR^6, SOR^6, $-SO_2R^6$, $-SO_2NR^9R^{10}$, $-CO_2R^8$, -N R^7R^8, or hetaryl optionally substituted by 1 or 2 groups independently selected from hydroxy, C_{1-6}alkoxy, halo, C_{1-6}alkyl, or C_{1-6}haloalkyl;

X is $-(CH_2)_q$- or C_{2-6} alkenylene;

q is an integer from 0 to 6;

R^6 and R^7 are independently selected from hydrogen, C_{1-6}alkyl, C_{3-7}cycloalkyl, aryl, hetaryl, hetaryl(C_{1-6}alkyl)- and aryl(C_{1-6}alkyl)- and R^6 and R^7 are each independently optionally substituted by 1 or 2 groups independently selected from halo, C_{1-6}alkyl, C_{3-7} cycloalkyl, C_{1-6} alkoxy, C_{1-6}haloalkyl, $-NHC(O)(C_{1-6}$alkyl), $-SO_2(C_{1-6}$alkyl), $-SO_2$(aryl), $-CO_2H$, and $-CO_2(C_{1-4}$alkyl), $-NH_2$, $-NH(C_{1-6}$alkyl), aryl(C_{1-6}alkyl)-, aryl(C_{2-6}alkenyl)-, aryl(C_{2-6}alkynyl)-, hetaryl(C_{1-6}alkyl)-, $-NHSO_2$aryl, -NH(hetarylC_{1-6}alkyl), $-NHSO_2$hetaryl,

-$NHSO_2(C_{1-6}alkyl)$, -NHC(O)aryl, or -NHC(O)hetaryl:

R^8 is selected from hydrogen, C_{1-6}alkyl and C_{3-7} cycloalkyl;

or R^7 and R^8, together with the nitrogen atom to which they are bonded, form a 5-, 6- or 7-membered nitrogen – containing ring;

R^9 and R^{10} are independently selected from hydrogen, C_{1-6}alkyl, C_{3-7}cycloalkyl, aryl, hetaryl, hetaryl(C_{1-6}alkyl)- and aryl(C_{1-6}alkyl)-, or R^9 and R^{10}, together with the nitrogen to which they are bonded, form a 5-, 6-, or 7- membered nitrogen containing ring;
and R^9 and R^{10} are each optionally substituted by one or two groups independently selected from halo, C_{1-6}alkyl, and C_{3-7}cycloalkyl, C_{1-6}haloalkyl;

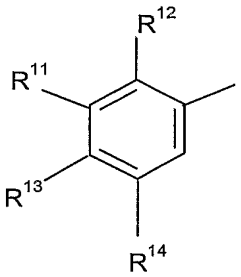
R^2 is selected from hydrogen, hydroxy, C_{1-6}alkyl, C_{1-6}alkoxy, halo, aryl, aryl(C_{1-6}alkyl)-, C_{1-6}haloalkoxy, and C_{1-6}haloalkyl;

R^3 is selected from hydrogen, hydroxy, C_{1-6}alkyl, C_{1-6}alkoxy, halo, aryl, aryl(C_{1-6}alkyl)-, C_{1-6}haloalkoxy, and C_{1-6}haloalkyl;

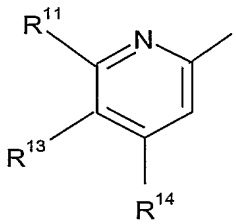
R^a and R^b are independently selected from hydrogen and C_{1-4} alkyl.

R^4 and R^5 are independently selected from hydrogen and C_{1-4} alkyl with the proviso that the total number of carbon atoms in R^4 and R^5 is not more than 4: and

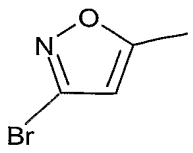
Ar^1 is a group selected from



(a)

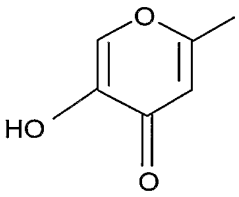


(b)



(c)

and



(d)

wherein R^{11} represents halogen, $-(CH_2)_nOR^{15}$, $-NR^{15}C(O)R^{16}$, $-NR^{15}SO_2R^{16}$, $-SO_2NR^{15}R^{16}$, $-NR^{15}R^{16}$, $-OC(O)R^{17}$ or $OC(O)NR^{15}R^{16}$,
and R^{12} represents hydrogen, halogen or C_{1-4} alkyl;

or R^{11} represents $-NHR^{18}$ and R^{12} and $-NHR^{18}$ together form a 5- or 6- membered heterocyclic ring;

R^{13} represents hydrogen, halogen, $-OR^{15}$ or $-NR^{15}R^{16}$;

R^{14} represents hydrogen, halogen, haloC_{1-4} alkyl, $-OR^{15}$, $-NR^{15}$ R^{16}, $-OC(O)R^{17}$ or $OC(O)NR^{15}R^{16}$;

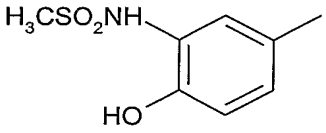
R^{15} and R^{16} each independently represents hydrogen or C_{1-4} alkyl, or in the groups $-NR^{15}R^{16}$, $-SO_2NR^{15}R^{16}$ and $-OC(O)NR^{15}R^{16}$, R^{15} and R^{16} independently represent hydrogen or C_{1-4} alkyl or together with the nitrogen atom to which they are attached form a 5-, 6- or 7-membered nitrogen-containing ring,

R^{17} represents an aryl group which may be unsubstituted or substituted by one or more substituents selected from halogen, C_{1-4} alkyl,
hydroxy, C_{1-4} alkoxy or halo C_{1-4} alkyl; and

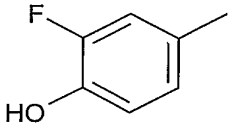
n is zero or an integer from 1 to 4;
provided that in the group (a), when R^{11} represents $-(CH_2)_nOR^{15}$ and n is 1, R^{13} is not OH.

2. A compound according to claim 1 wherein Ar^1 is selected from group (a) or group (b), as defined in claim 1.

3. A compound of formula (I) according to claim 2 wherein group (a) is selected from a group of formula (iv) or (xix):

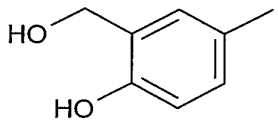


(iv)



(xix)

4. A compound of formula (I) according to claim 2 wherein group (b) is a group of formula (iii):



(iii)

5. A compound of formula (I) according to any of claims 1-4 wherein R^1 is selected from hydrogen, C_{1-4}alkyl, hydroxy, cyano, C_{1-6}alkoxy, halo, XCO_2R^8, XNR^6COR^7, $XCONR^7R^8$, $-NR^6C(O)NR^7R^8$, $XSOR^6$, $XNR^6SO_2NR^7R^8$, $XNR^6SO_2NR^7CO_2R^7$ and $-NR^6SO_2R^7$
wherein R^6 and R^7 are as defined above.

6. A compound of formula (I) according to claim 5 wherein R^1 is selected from $XC(O)NR^7R^8$ or hydrogen.

7. A compound of formula (I) according to any of claims 1-6 wherein R^2 and R^3 each represent hydrogen.

8. A compound of formula (I) according to any of claims 1-7 wherein R^4 and R^5 each represent hydrogen.

9. A compound of formula (I) according to any of claims 1-8 wherein R^a and R^b each represent hydrogen.

10. A compound of formula (I) according to claim 1 which is selected from:
3-{[2-(4-{2-[((2*R*)-2-hydroxy-2-{4-hydroxy-3-[(methylsulfonyl)amino]phenyl}ethyl)amino]ethyl}phenoxy)ethoxy]methyl}benzamide;
N-{2-hydroxy-5-[(1*R*)-1-hydroxy-2-({2-[4-(4-phenylbutoxy)phenyl]ethyl}amino)ethyl]phenyl}methanesulfonamide;
N-(5-{(1*R*)-2-[(2-{4-[2-(benzyloxy)ethoxy]phenyl}ethyl)amino]-1-hydroxyethyl}-2-hydroxyphenyl)methanesulfonamide;
3-({2-[4-(2-{[(2*R*)-2-(3-fluoro-4-hydroxyphenyl)-2-hydroxyethyl]amino}ethyl)phenoxy]ethoxy}methyl)benzamide;
4-{(1*R*)-2-[(2-{4-[2-(benzyloxy)ethoxy]phenyl}ethyl)amino]-1-hydroxyethyl}-2-fluorophenol;
2-fluoro-4-[(1*R*)-1-hydroxy-2-({2-[4-(4-phenylbutoxy)phenyl]ethyl}amino)ethyl]phenol;
3-[(2-{4-[2-({2-hydroxy-2-[5-hydroxy-6-(hydroxymethyl)pyridin-2-yl]ethyl}amino)ethyl]phenoxy}ethoxy)methyl]benzamide;
6-{2-[(2-{4-[2-(benzyloxy)ethoxy]phenyl}ethyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)pyridin-3-ol;
2-(hydroxymethyl)-6-[1-hydroxy-2-({2-[4-(4-phenylbutoxy)phenyl]ethyl}amino)ethyl]pyridin-3-ol;

and salts, solvates and physiologically functional derivatives thereof.

11. A method for the prophylaxis or treatment of a clinical condition in a mammal, such as a human, for which a selective β_2-adrenoreceptor agonist is indicated, which comprises administration of a therapeutically effective amount of a compound of formula (I), according to any of claims 1-10, or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof.

12. A compound of formula (I), according to any of claims 1-10, or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof for use in medical therapy.

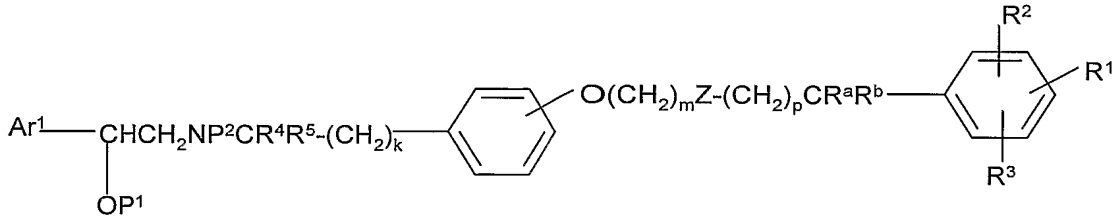
13. A compound of formula (I), according to any of claims 1-10, or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof for use in prophylaxis or treatment of a condition for which a selective β_2-adrenoreceptor agonist is indicated.

14. A pharmaceutical formulation comprising a compound of formula (I), according to any of claims 1-10, or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof, and a pharmaceutically acceptable carrier or excipient, and optionally one or more other therapeutic ingredients.

15. The use of a compound of formula (I), according to any of claims 1-10, or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof in the manufacture of a medicament for the prophylaxis or treatment of a clinical condition for which a selective β_2-adrenoreceptor agonist is indicated.

16. A process for the preparation of a compound of formula (I), according to any of claims 1-10, or a salt, solvate, or physiologically functional derivative thereof, which comprises:

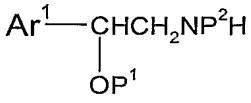
(a) deprotection of a protected intermediate, for example of formula (II):



(II)

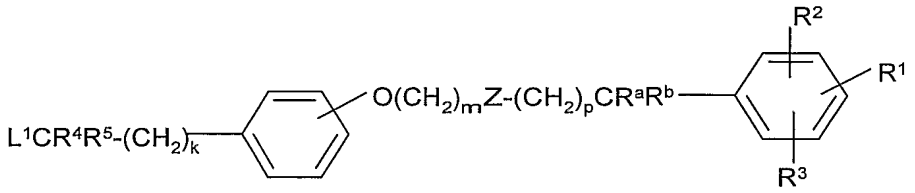
or a salt or solvate thereof, wherein Ar^1, R^1, R^2, R^3, R^a, R^b, R^4, R^5, Z, k, m, and p are as defined for the compounds of formula (I), and P^1 and P^2 are each independently either hydrogen or a protecting group provided that at least one of P^1 and P^2 is a protecting group; or

(b) alkylation of an amine of formula (XIII)



(XIII)

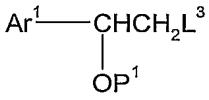
wherein Ar^1 is as defined above for compounds of formula (I) and P^1 and P^2 are each independently either hydrogen or a protecting group,
with a compound of formula (XIV):



(XIV)

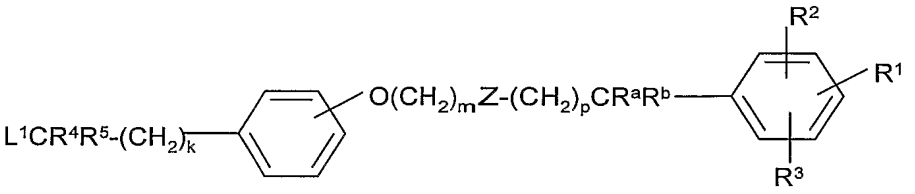
wherein R^1, R^2, R^3, R^4, R^5, R^a, R^b, Z, m, and p are as defined for the compound of formula (I) and L^1 is a leaving group;

(c) reacting a compound of formula (XV):



(XV)

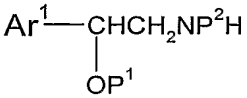
wherein P^1 and Ar^1 are as hereinbefore defined and L^3 is a leaving group, with an amine of formula (XVI):



(XIV)

wherein R^1, R^2, R^3, R^4, R^5, R^a, R^b, Z k, m, p and P^2 are as hereinbefore defined; or

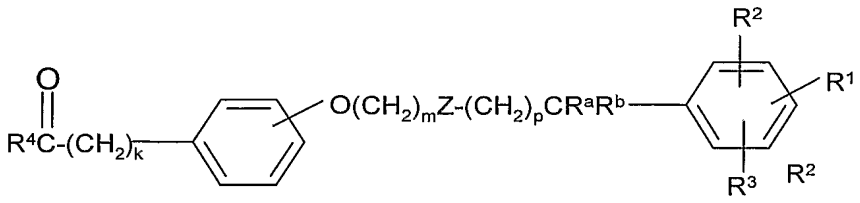
d) reacting a compound of formula (XIII):



(XIII)

as hereinbefore defined,

with a compound of formula (XVII):



(XVII)

under conditions suitable to effect reductive amination.

followed by the following steps in any order:

(i) optional removal of any protecting groups;

(ii) optional separation of an enantiomer from a mixture of enantiomers;

(iii) optional conversion of the product to a corresponding salt, solvate, or physiologically functional derivative thereof.